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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,951	02/06/2004	David Agus	39740-0009A	8470

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EXAMINER	
SCHLAPKOHL, WALTER	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 07/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/773,951	AGUS ET AL.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	wls

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-54* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10, 13-15, 25-31, 35-50 and 52-54, drawn to methods of prognosis of treatments with an EGFR inhibitor comprising determining the expression level of **one or one combination of RNA transcripts** selected from the group consisting of STAT5A, STAT5B, WISP1, CKAP4, FGFR1, cdc25A, RASSF1, G-Catenin, H2AFZ, NME1, NRG1, BCl2, TAGLN, YB-1, Src, IGF1R, CD44, DIABLO, TIMP2, AREG, PDGFRa, CTSB, Hepsin, ErbB3, MTA1, Gus and VEGF; wherein overexpression of **one or one combination** of transcripts selected from the group consisiting of STAT5A, STAT5B, WISP1, CKAP4, FGFR1, cdc25A, RASSF1, G-Catenin, H2AFZ, NME1, NRG1, BCl2, TAGLN, YB-1, Src, IGF1R, CD44, DIABLO, TIMP2, AREG, PDGFRa and CTSB indicates a patient will NOT respond well to said treatment; and overexpression of **one or one combination of different RNA transcripts** selected from the group consisting of Hepsin, ErbB3, MTA1, Gus and VEGF indicates that the patient is likely to

respond well to said treatment and a kit for such a method, classified in class 435, subclass 6.

II. Claims 1-9, 11-12, 14-15, 35-38, 46-48 and 50-54, drawn to methods of prognosis of treatments with an EGFR inhibitor comprising determining the expression level of **one or one combination of RNA transcript "expression products"** selected from the group consisting of STAT5A, STAT5B, WISP1, CKAP4, FGFR1, cdc25A, RASSF1, G-Catenin, H2AFZ, NME1, NRG1, BCl2, TAGLN, YB-1, Src, IGF1R, CD44, DIABLO, TIMP2, AREG, PDGFRa, CTSB, Hepsin, ErbB3, MTA1, Gus and VEGF; wherein overexpression of **one or one combination of transcript "expression products"** STAT5A, STAT5B, WISP1, CKAP4, FGFR1, cdc25A, RASSF1, G-Catenin, H2AFZ, NME1, NRG1, BCl2, TAGLN, YB-1, Src, IGF1R, CD44, DIABLO, TIMP2, AREG, PDGFRa and CTSB indicates a patient will NOT respond well to said treatment; and overexpression of **one or one combination of different RNA transcript "expression products"** selected from the group consisting of Hepsin, ErbB3, MTA1, Gus and VEGF indicates that the patient is likely to respond well to said treatment and a kit for such a method, classified in class 435, subclass 7.1.

III. Claims 16-24, drawn to an array as the claims read on polynucleotides hybridizing to **one combination** of genes selected from STAT5A, STAT5B, WISP1, CKAP4, FGFR1, cdc25A, RASSF1, G-Catenin, H2AFZ, NME1, NRG1, BCl2, TAGLN, YB-1, Src, IGF1R, CD44, DIABLO, TIMP2, AREG, PDGFRa, CTSB, Hepsin, ErbB3, MTA1, Gus and VEGF, classified in class 435, subclass 287.2.

IV-XXX. Claims 32-34, drawn to a method for amplification of **one** gene using **one** amplicon from Table 3 and **one** primer-probe set from Table 4 and the corresponding polynucleotide(s), classified in class 435, subclass 91.2.

The inventions are distinct, each from the other, for the following reasons:

Groups I-XXX are comprised of multiple independent and/or distinct inventions recited in the alternative which are the products or methods drawn to different polynucleotides/polypeptides which do not render obvious each other and thus are patentably distinct. Applicant must elect a single invention which is the product or method drawn to one specific polynucleotide/polypeptide combination to which the

claims will be restricted. Applicant must also indicate which claims are readable on the elected invention. This is not an election of species because the polynucleotides/polypeptides are different and distinct and thus the methods drawn to different and distinct polynucleotides/polypeptides are different and distinct inventions from each other.

Note: the non-standard format of this restriction, separating the inventions into multi-invention groups drawn to independent or distinct combinations of polynucleotides and polypeptides, followed by an election of a single invention drawn to one combination of polynucleotides or polypeptides within the elected multi-invention group, was done for the sake of compactness of the communication and clarity, instead of using the more standard format setting forth each separate invention drawn to each separate sequence which would require a much longer communication.

For related process inventions, the inventions are distinct if (a) the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; (b) the inventions as claimed are not obvious variants; and (c) the inventions as claimed are either not capable of use together or can have a materially different

design, mode of operation, function or effect. See MPEP § 802.01.

The methods of Groups I and II and Groups IV-XXX do not overlap in scope because the Group I invention comprises isolating cellular RNA from a sample and quantifying the levels of transcript in the sample; the Group II invention comprises the use of immunohistochemistry or proteomics technology to determine the level of "transcript products" from the sample; and the Group IV-XXX inventions comprises amplification of a gene. Thus, Group I, Group II and the Group IV-XXX inventions have a materially different design, mode of operation and/or effect since the Group I and II biomarkers are chemically and structurally different, and the Group IV-XXX inventions rely on the use of primers for amplification of a nucleic acid. Moreover the Group I, Group II and Group IV-XXX inventions are not obvious variants because, for example, the determination of transcript levels as in Group I does not necessarily correlate with protein/transcript product levels as in Group II and method of amplification of Groups IV-XXX are not necessarily required for the Group I invention. Therefore, the methods are not obvious variants over each other.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in

the art in view of their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Inventions III and Inventions IV-XXX are directed to related products. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the inventions of Groups III and IV-XXX do not overlap in scope because the Group III invention is comprised of polynucleotides hybridizing to genes immobilized on a solid surface and each of the Group IV-XXX inventions is comprised of a polynucleotide and its corresponding primer-probe set in any setting or condition. The inventions of Group III and Groups IV-XXX are not obvious variants due to their completely different structures and chemical properties: Group III comprises DNA immobilized to a solid surface and the Group IV-

XXX inventions comprise primers not present in the Group III invention. The Group III and Group IV-XXX inventions also have a completely different design and mode of operation; for example, the Group III array has multiple polynucleotides immobilized on a solid surface useful for detection of gene expression while the polynucleotides of the Group XXXI-LVII inventions are utilized for polynucleotide amplification.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Inventions I and III are related as processes and products for their practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the process of Group I as claimed can be practiced by utilizing

any combination of polynucleotides present on any of the different arrays encompassed by the Group III arrays. For example, the Group I invention could be practiced with an array comprising STAT5A and STAT5B or with an array comprising CKAP4 and VEGF.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Except for the specific relationships above, the inventions of Groups II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 808.01). In the instant case the method of Group II is not disclosed as capable of use together with the polynucleotide array of Group III and the Group II invention has a different mode of operation which utilizes transcript expression products as opposed to

polynucleotides and the array of Group III has not been disclosed as capable of use with such transcript expression products.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species:

1. type of cancer/cancer cell utilized (choose from ovarian cancer, colon cancer, pancreatic cancer, non-small cell lung cancer, breast cancer, and head and neck cancer as in claims 6, 29-30, 36 and 38);

2. type of EGFR inhibitor (choose from a) an antibody or antibody fragment as in claim 14 *or* b) a small molecule as in claim 15); and

3. a method of analysis/normalization for the sample (choose from a) normalization with **one or one combination** of housekeeping genes as in claims 39-40 *or* b) global gene expression analysis as in claims 41-45).

The species are independent or distinct because the types of cancers are not obvious variants over one another as gene expression patterns are not the same from cancer to cancer. Furthermore, the choice of EGFR inhibitor may have an important effect on the gene expression patterns central to the invention. In addition, the method of normalization/analysis regarding gene expression can have a large impact upon which levels of expression are found to be high relative to a test sample.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 25, 35 and 37 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims

readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, Applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during

prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

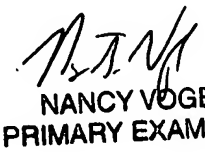
Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily

from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at (800) 786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Thursday from 8:30 AM to 6:00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.



Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

June 11, 2006